ASSESSMENT AND APPLICATION OF THE MULTISTATE LIFE TABLES APPROACH TO MODELING POPULATION HARM REDUCTION WITH SMOKELESS TOBACCO

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ABSTRACT

Purpose: To identify and evaluate assumptions underlying the multistate life tables approach for estimating differences in population life expectancy due to different distributions of harmful exposures.

Methods: A published analysis that used multistate life tables to calculate life expectancy under different exposure scenarios was evaluated to delineate source data and underlying assumptions, and efforts were undertaken to replicate and improve analysis findings using

Results: Limitations of the published analysis included risk estimates from one population applied to a dissimilar target population, resulting in lower risks for exposed than unexposed in some groups; use of identical input risk estimates for dissimilar diseases, resulting in invalid effect sizes; and failure to account for time dependent effects of exposure and removal from exposure, resulting in overestimated effects. Nevertheless, efforts to replicate analysis findings and address potential limitations yielded comparable estimates of differential life expectancies based on different exposure scenarios.

Discussion: While the life tables approach can provide important information regarding population life expectancy under different exposure scenarios, clear documentation and/or modification of underlying assumptions for testing the effect of alternate assumptions can

BACKGROUND

Discussions about potentially reduced exposure tobacco products (PREPs) often include statements that current smokers may choose to substitute PREPs for some or all of their cigarettes instead of quitting tobacco use, and that non-smokers may choose to begin using PREPs instead of remaining tobacco-free. Snüs, a low nitrosamine smokeless product, is a PREP that is currently available in some areas. Because they are not exposed to combustion products, snüs users are expected to be at lower risk than cigarette smokers of smoking-related diseases. Gartner et al.1 used life tables techniques to estimate the numbers of never smokers and former smokers who must begin using snüs to offset the gain in aggregate life expectancy due to current smokers switching to snüs and potential new smokers choosing snüs instead of cigarettes.

To identify and evaluate the methods and assumptions underlying in the Gartner et al. multistate life tables approach, we completed a thorough critical review of their paper and related publications. We modified their methods to address shortcomings we identified, and evaluated the effect of the changes on the calculated results to assess the sensitivity of the approach to alternative source data and risk estimates.

RESULTS

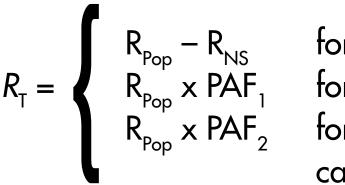
Gartner et al.¹ created life tables, separately for men and women, to compare the disability-adjusted life expectancies of five groups of Australian adults, aged 35 to 80:

- (i) never tobacco users;
- (ii) current smokers; (iii) former smokers;
- (iv) former smokers who initiated snüs; and
- Age- and gender-specific rates for selected causes of death were adjusted
- to estimate the proportions presumed to be tobacco-related: cancers of the lung, upper aerodigestive tract, pancreas, bladder and
- chronic obstructive pulmonary disease (COPD);

(v) never tobacco users who initiated snüs.

- other non-cancer respiratory disease; and
- cardiovascular disease (CVD)

Tobacco-related mortality rates, R_T, were defined by Gartner et al. 1 as:



= cause-specific mortality rate in the target population R_{NS} = lung cancer mortality rate among non-smokers

PAF, and PAF, are the population attributable fractions, defined as the estimated proportions of tobacco-related diseases that are due to tobacco exposure vs. other causes (accounting for the proportion of smokers and snüs users in the population). The relative risk of snüs vs. current smoking was 0.8, based on consensus estimates published by Levy et al.²

Several shortcomings in documentation and underlying assumptions made it impossible to replicate or directly apply the calculations as described

Assumes a five year latent interval for non-cancer respiratory diseases

diminished to zero after 5 years of not smoking. Observational data

Disease-specific mortality rates are readily available from the CPS-

II⁴, and could have been used to calculate disease-specific SIRs for

non-lung cancers and COPD. The SIR calculation is also affected by

the incongruity between the lung cancer mortality rates for CPS-II

Gartner et al. did not explain why the relative risks for only three

causes of death (lung cancer, COPD and CVD) were considered

valid estimators of the relative risks for all causes of death under

consideration, nor did they discuss the implications of this approach

for the magnitude and precision of their risk estimates. Publications

discussing CPS-II provide disease-specific comparisons of risks for

current smokers and former smokers that could have been used in the

compared to the Australian population, noted above.

and COPD attributable to smoking, and the risk due to smoking is

suggest a more complex picture³.

life table calculations⁴.

TABLE 1. Description of problematic methods and calculations used by Gartner et al.

Discussion Lung cancer mortality rate among never smokers was obtained CPS-II data could not have been used as described by Gartner et from the American Cancer Society Cancer Prevention Study II al., because the lung cancer mortality rate among 35-40 year old nonsmokers in the CPS-II population exceeds the lung cancer rate (CPS-II) and used to estimate the lung cancer mortality rate amon for 35-40 year old Australian smokers and nonsmokers, combined. never smokers in Australia. Therefore, the calculation of tobacco-attributable lung cancer described by Gartner et al. for this age group would return an impossible, negative value.

- 2. The prevalence of smoking in 1995, five years prior to the baseline year for mortality calculations, was used to calculate tobacco-attributable mortality due to non-cancer respiratory an cardiovascular disease.
- 3. Lung cancer mortality rates from the CPS-II study were used to calculate the smoking impact ratio (SIR) used in estimating the tobacco-related population attributable fraction of mortality due to non-lung cancers and COPD.
- 4. The tobacco attributable mortality risk in current smokers compared to former smokers was derived from relative risk estimates comparing risks of lung cancer, COPD (applied to all non-lung cancers) and CVD (also applied to non-cancer
- respiratory diseases) for current vs. former smokers in CPS-II.
- 5. The method for estimating risk reversal for former compared to current smokers was not clearly described.

Risk reversal, RR_{TES vs. CS}, may be applied as an average benefit to all former smokers compared to current smokers, or an arbitrary average quitting age may be selected and a progressive benefit (a decay function) applied to subsequent age intervals to reflect greater benefit with additional years of cessation. If duration of cessation is considered, then an arbitrary age at cessation must be specified. Gartner et al. did not explain the method used to calculate risk

6. Age-specific probability of disability not available as described.

Age-specific data published in the Australian Burden of Disease study⁵ were published in groups not comparable to those described by Gartner et al. The methods for calculating the probability of agerelated, age-specific disability and disease severity weights were not specified. The stage of disease (terminal or pre-terminal) was not specified in the discussion of severity weighting.

Gartner et al. seem, based on their bibliography, to have used data on disability due to tobacco-related diseases that was calculated using the DISMOD computer program⁶. DISMOD can use estimates of incidence, mortality, and duration of disease to produce estimated duration of disease-related disability. Neither the source nor the values of the input parameters required by DISMOD were specified by Gartner et al.

7. Disease severity weighting methods were not described.

Gartner et al. did not specify how severity weights were applied to

8. The calculation of population "break even" points was not explained, and no intermediate calculations were provided. adjusted person-years, or which stage of disease (terminal vs. preterminal) was used in selecting the severity weight.

Had intermediate calculations been provided, verification of assumptions and inferences needed (due to the lack of documentation) to replicate the analyses would have been possible.



Gartner et al.

Hill, DJ, 1998

COPD: CPS-II

Stroke: CPS-II

CHD: CPS-II

Levy, 2004

AIHW

CPS-II

CPS-II

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CPS-II, Thun, 2000

All cancer outcomes used

CPS-II lung cancer data

We made three changes to the Gartner et al. approach:

the benefits of quitting smoking.

TABLE 2. Source of Inputs

Prevalence of current smokers

Disease risk for current smokers vs. never smokers

Disease risk for former vs. current smokers

Disease risk for snüs users vs. current smokers

Age-sex specific mortality rate for never smokers

Age-sex specific mortality rate for lifelong smokers

Age-related, non-tobacco related health adjustment factor Mathers

b http://www.cdc.gov/mmwr/preview/mmwrhtml/mm5644a2.htm

National age-sex specific mortality rate

Mortality Rate

Prevalence Rate

^a MMWR 2007;56(38):933-6

c http:/www.seer.cancer.gov/csr/1975_2005/

INPUT

(i) Used baseline mortality data for the US population instead of the (ii) Used disease-specific risks for cancers rather than applying the lung

cancer risks to all smoking-related cancers; and i) Applied a decay function instead of a constant function to describe We selected more appropriate model inputs: Cause-specific mortality estimated from the Kaiser-Permanente Cohort

Study vs. CPS-II to improve external internal and external validity; and Age-specific probability of disease.

SOURCE

We also replaced subjective quality of life adjustments with average duration of disease, which can be objectively estimated for any population with adequate data.

Sulsky et al.

Cancers:

CPS-II, Thun, 2000⁷

Lung- CPS-II⁷

COPD: CPS-II⁷

CHD: CPS-II⁷

Levy, 2004²

Mathers¹³

CDC^a, US Census

Pancreas-Fuchs, 19968

Upper Aero- Wynder, 1977¹⁰

Kidney- Parker, 20039

Stroke: Wanamethree, 1995¹¹

Kaiser-Permanente Cohort Study¹²

Kaiser-Permanente Cohort Study¹²

Lung, Upper Aero, Pancreatic, Bladder,

Kidney Cancers: SEER CSR 2005°

COPD: CDC MMWR Surveillance

CDC Deaths - Final 2004a

IHD, Stroke: NHIS 2006b

Each of the modifications was applied to US population data and used to calculate two "break even" points for comparison with the estimates derived by Gartner et al. (Table 3 and Table 4).

TABLE 3. How many never-smokers and former smokers must start using snüs to offset the surplus life expectancy due to current smokers switching to snüs instead of continuing to smoke cigarettes?

Cessation benefit model	Kaiser-Permanente Referent		CPS-II Referent	
	Men	Women	Men	Wome
Constant	28.7	16.9	16.7	16.6
Decay	35.2	37.7	18.2	19.5
Gartner et al [†] .	_	_	17.0	21.0

- Depending on the cessation benefit model (constant vs. decay) and referent population (Kaiser vs. CPS-II), between ~17 and 38 people who never smoked or who quit smoking cigarettes must begin using snüs to offset the gain in population life expectancy due to one current smoker switching from cigarettes to snüs instead of continuing to smoke cigarettes.
- The model was more sensitive to changing the referent population than to alternative methods of calculating the smoking cessation benefit. Using the Kaiser-Permanente Cohort study as a referent population to calculate mortality resulted in higher estimated break even points for both men and women.

TABLE 4. How many non-users of tobacco must begin using snüs to offset the gain in population life expectancy due to one potential smoker who chooses to use snüs instead of cigarettes?

	Kaiser-Permanente Referent		CPS-II Referent	
	Men	Women	Men	Women
Constant or Decay	11.8	1 <i>7</i> .8	16.4	15.8
Gartner et al.	_	_	21.0	20.0

 A minimum of 12 men and 16 women who do not use tobacco must begin using snüs to offset the surplus life expectancy due to one potential smoker who chooses to use snüs instead of cigarettes.

 Using the Kaiser-Permanente Cohort study as a referent population to calculate mortality resulted in lower estimated break even points compared to calculations based on the CPS-II mortality rates.

DISCUSSION

It was not possible to exactly replicate the calculations of Gartner et al. due to deficiencies in the documentation

Some of the assumptions and source data used by Gartner et al. were

- The CPS-II study provides mortality rates that suggest improved life expectancy for smokers compared to non-smokers in some age groups and when applied to other populations;
- Disease risks and smoking cessation benefits are expected to differ by disease, but Gartner et al. used lung cancer rates for all cancers
- Smoking cessation benefits are expected to differ by length of time since quitting smoking, but a constant cessation benefit may have been applied by Gartner et al.

Our closest approximation to the methods of Gartner et al. resulted in similar magnitude results for estimated break even points.

The results were most sensitive to the choice of population used to estimate underlying mortality rates for smokers compared to nonsmokers, and less sensitive to the inputs used to calculate the exposure-specific relative risks and tobacco-attributable fractions.

The life tables approach is onerous to fully document and inputs are difficult to modify, e.g., to complete sensitivity analyses. The life tables approach does not easily model time-dependent changes in risk, such as the increasing risk of all causes of death associated with age, and the decline in risk of smoking-related diseases associated with duration of

SUMMARY

In spite of differences in the absolute magnitude of the estimated break even points, all calculations suggested an increase in population life expectancy when fewer people are exposed to tobacco combustion products. Under the present model:

Approximately 17 potential former smokers (men or women) must choose snüs instead of quitting smoking to offset the gain in life expectancy due to one current smoker switching to snüs instead of continuing to smoke cigarettes.

> start using snüs to offset the gain in life expectancy due to one potential smoker who instead became a snüs user.



Based expert consensus estimates (2), all calculations assumed that snüs provides lower risk than cigarettes. This is expected to be due to the absence of exposure to tobacco combustion products associated with snüs use. However, new data may emerge to refute or modify this assumption. This is one example of why it is important to develop a model whose inputs are easily modified.

We are developing a dynamic population model to allow flexibility for the user to specify and easily document all model inputs and underlying assumptions, including population distributions of exposure and associated risk estimates, to assess the effect of changes in these quantities on population life expectancy under different scenarios and with application to any target population.

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